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Study Closeout at Research Sites

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The activities conducted at the end of a clinical study constitute "study closeout." Proper closeout ensures that study records are collected and archived, left-over test articles, equipment and study materials are returned to the sponsor or disposed of, and any loose ends are tied up. Sponsors often hold final payment until after closeout. FDA inspections after closeout proceed more smoothly when everything is in order.

Studies may be closed when all study subjects have completed the study, the principal investigator decides to stop participating in the study, or the sponsor terminates the study or the site. Close a study as soon as possible, before study personnel and subjects move on, documents drift off, and memories fade. As with everything else, the principal investigator is responsible for ensuring that the study is properly closed. The study coordinator(s), regulatory specialist(s), and other study personnel all have a role to play.

The activities below are typical, but review the study protocol, clinical trial agreement, and site standard operating procedures (SOPs) for unusual requirements.

Closeout Activities

Complete the following activities to closeout a study:

- Follow-up on serious adverse events (SAEs) and clinically significant abnormal lab values and clinical observations for at least thirty days after the subject completes the study. If not resolved at the end of the period, document in the source documents, and notify the sponsor.
- Lineout, initial and date any empty comment fields in source documents.
- Complete all case report forms (CRFs) and transmit them to the sponsor.
- Respond to all open requests for data corrections or verifications on CRFs. Document unresolvable queries. After all data queries have been resolved, check study files for completeness.
- Collect all study drug and equipment from study subjects.
- Inventory all used and unused study drug. Reconcile or explain discrepancies, if any.
- Inventory any stored lab specimens and determine their disposition.
- Inventory all sponsor-provided equipment and determine its disposition.
- Return drugs, empty containers, supplies, devices and equipment to the sponsor per its instructions, unless instructed to retain or destroy them by the sponsor. Include packing slips with shipments. Retain copies of shipping documentation.
- File copies of drug logs, final inventory, and shipping documents in the regulatory binder. File a copy of the sponsor's drug disposal authorization, if any, in the regulatory binder.
- If the randomization code on any study drug was broken for any reason, ensure that complete documentation is in the regulatory binder.
- Obtain updated financial disclosure forms from the investigator and any subinvestigators.
- Complete all other sponsor-required reports in a timely manner. File copies in the regulatory binder.

- Review the regulatory binder. Ensure that all documents are in their correct places. Complete incomplete documents and recover any missing documents, or place an explanatory note-to-file in the regulatory binder.
- On the subject completion form and in medical charts, document subject completion of their participation in the study. Remove from the subjects' medical charts any medication restrictions or study warnings, if applicable.
- Complete the IRB annual renewal form indicating "final" or "closure" and submit the report. Include a short narrative summary of the conclusion of the study at the site. Include comments on any adverse events (AEs) that occurred and the significance they may have had on study findings. Provide a copy of the report to the sponsor and file it in the regulatory binder.
- For each subject, the principal investigator signs an investigator statement confirming that all data for that subject is complete and accurate.
- Take down any subject recruiting posters and website postings.
- Notify subinvestigators, pharmacy, clinical lab, accounting office, and other departments that the study has been completed, with appropriate closeout instructions, e.g., for disposing of study materials and collecting payment.
- Conduct study closeout visit. (See below.)
- Package all study documentation for storage. Include an inventory statement. Archive all study documentation in a secure location, ensuring that it will be stored for the period of time specified in the clinical trial agreement.
- Ask the sponsor for written permission to break the blind and provide treatment information for subjects.[1]
- Once any open items are resolved, obtain a closeout letter from the sponsor and file it in the regulatory binder.

Closeout Visits

Before the visit:

- Ensure that all routine monitoring issues have been addressed.
- Arrange a mutually convenient date, time, duration and agenda for the site monitor to conduct the closeout visit for the final review of regulatory files, source data verification, drug accountability reconciliation, and review of the record storage plan, as soon as practical after the last subject has completed all scheduled visits,
- Ensure that all regulatory documentation, source documents, and case report forms are complete and available for review.
- Ensure that all data queries have been resolved to the extent possible.
- Ensure that subject medical records will be available for review.
- Inventory and reconcile all study drug and equipment.

During the closeout visit:

- Ensure that all study personnel are available to resolve any open issues.
- Ensure that the site monitor signs the visitor log.
- Give the site monitor access to all documents required to complete the closeout visit.
- Discuss any study-related issues.
- Discuss the possibility of a sponsor audit or FDA inspection.
- Conduct joint visits to the drug storage area(s) and review drug accountability records.

- Preferably, ship left-over study drug and equipment in the site monitor's presence.
- Return randomization codes.
- Determine disposition of unused CRFs and clinical supplies.
- Inform site monitor of storage location of study records.
- If data were entered on computers, determine when hard copies of CRFs will be provided to the site and review the sponsor's plan for protecting the integrity of the electronic data.
- Discuss with the site monitor the sponsor's requirements for subject follow-up for SAEs after closeout.
- Discuss the possibility of publication of the data and participation in future studies.
- If appropriate, provide the final closeout report. If there are any open issues, discuss them and arrange for follow-up.
- Identify points of contact for new issues that may arise, such as data queries and inspections.

Study Post Mortems

Upon completion of a study, hold a "post mortem" meeting with all study personnel to identify what went right and what went wrong in the study. What should or should not be done in future studies?

Many topics can be discussed, such as:

- Which recruiting methods worked best? Which did not work?
- Which eligibility criteria were problems?
- Were there any retention problems?
- Which study activities took more or less time than expected?
- Did the sponsor or IRB have any unusual requirements or pose any unusual challenges?
- Did any technology pose problems?
- Was the study profitable? Why?
- Should the site's SOPs be modified?
- Would additional training have been helpful?

Add the findings to an accessible database and modify training programs as appropriate.

Note

1. "Investigators are encouraged to communicate a summary of the trial results, as appropriate, to their research participants after conclusion of the trial." PhRMA Principles on Conduct of Clinical Trials and Communication of Clinical Trial Results (4e) http://www.phrma.org/files/Clinical%20Trials.pdf

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